Remarks

Claims 35-50 are pending. Claims 1-34 were previously cancelled without prejudice to or disclaimer of the underlying subject matter. Claim 50 has been amended. New claims 51 and 52 have been added. Support for the amendments can be found throughout the specification and claims as originally filed, for example on page 21, line 17 through page 22, line 4, and in the original claims. No new matter enters by this amendment. Upon entry of the foregoing, claims 35-52 will be pending.

I. Status of Prosecution

An appeal brief was filed on May 6, 2005. The Examiner indicates in the Office Action, however, that "[i]n view of the appeal brief filed on 05/06/2005, PROSECUTION IS HEREBY REOPENED." Office Action at page 2. Moreover, the Examiner indicates that "[n]ew grounds of rejection are set forth" in the Office Action. *Id.* The Examiner also requires the Applicant to either: "(1) file a reply under 37 CFR 1.111...; or (2) request reinstatement of the appeal." *Id.* Applicants acknowledge that prosecution has been reopened in the present Office Action and Applicants submit the instant amendment and response under 37 CFR 1.111.

II. Rejection under 35 U.S.C. § 112 - New Matter

Claim 50 stands rejected under 35 U.S.C. § 112, first paragraph as allegedly "[containing] subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention." Office Action at page 3.

The Examiner alleges that "[c]laim 50 with the recitation of 'primer pair and a corresponding labeled probe which hybridizes under stringent conditions to a nucleic acid molecule of a 3' end of the Pisum sativum rbcS E9 gene' is not supported in the specification and raised the issue of new matter." *Id.* The Examiner further contends that "Applicants also did not point to written support for this parameter" and therefore constitutes new matter. *Id.* Applicants respectfully disagree.

The specification supports the claim language "primer pair and a corresponding labeled probe which hybridizes under stringent conditions to a nucleic acid molecule of a 3' end of the Pisum sativum rbcS E9 gene.' For example, the specification discloses "a primer pair and corresponding probe are designed which hybridize to a 3' end of the *Pisum sativum* rbcS E9 gene." Specification at page 36, lines 22-23. Moreover, the specification discloses various hybridization conditions, including stringent conditions. *See, e.g.*, Specification at page 12, line 12 through page 13, line 18. As such, the claim language is fully supported in the specification and does not constitute new matter.

Although Applicants disagree with the rejection, to facilitate prosecution claim 50 has been amended to recite "a 3' untranslated sequence of a 3' end of the *Pisum sativum* rbcS E9 gene." As such, the rejection of claim 50 for alleged new matter is moot and reconsideration and withdrawal of this rejection is requested.

III. Rejection under 35 U.S.C. § 112, first paragraph, Written Description

Claim 50 stands rejected under 35 U.S.C. § 112, first paragraph because the claimed subject matter allegedly was "not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the

application was filed, had possession of the claimed invention." Office Action at pages 4-5. Applicants respectfully traverse this rejection.

More particularly, the Examiner argues that "[t]he claim broadly encompasses any sequences that will hybridize to 'a' nucleic acid of 'a' 3' end of the *Pisum sativum* rbcS E9 gene which encompass nucleic acid sequences that are not limited to SEQ ID NO: 2, 7-9 and 28." *Id.* at page 5. Apparently, the Examiner contends that "the specification does not describe the 3' end of the P. sativum rbcS E9 gene nor the entire gene of rbcS E9 gene." *Id.* The Examiner argues that "the claim [encompasses] an extremely large genus of polynucleotides, wherein the specification's disclosure of a single sequence of SEQ ID NO: 2, which describes only the 3' untranslated end of P. sativum rbcS E9 gene which is not representative of this genus." *Id.* The Examiner argues that an "[a]dequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it" and that "[t]he nucleic acid itself is required." Office Action at page 7. Applicants respectfully disagree.

The Federal Circuit has recently held that Applicants need not re-describe that which is already known. *Capon v. Eschar*, 418 F.3d 1349 (Fed. Cir. 2005) ("Board erred in holding that the specifications do not meet the written description requirement because they do not reiterate the structure or formula or chemical name for the nucleotide sequences of the claimed chimeric genes"). The *P. sativum* rbcS E9 nucleotide sequence has been described previously, for example in Coruzzi, G., *et al.*, *EMBO J.*, 3:1671-1679 (1984). Moreover, the specification discloses the nucleic acid sequence of the 3' untranslated region of the *P. sativum* rbcS gene. *See, e.g.*, SEQ ID NO: 2. The claim at issue is

directed to an amplification kit for the detection of a transgenic nucleic acid molecule comprising, *inter alia*, a labeled probe which hybridizes under stringent conditions to a nucleic acid molecule of a 3' end of the *Pisum sativum* rbcS E9 gene.

In addition, the specification provides further disclosure such that a person of ordinary skill in the art would, after reading the present specification, understand that Applicants had possession of the claimed invention. For example, the specification describes gene sequences, corresponding sequences, preferred sequences, and so forth of the *Pisum sativum* rbcS E9 gene (*see, e.g.,* specification at page 26, line 1 through page 28, line 14; in the Sequence Listing; and in the claims as originally filed). The specification also describes appropriate hybridization conditions (*see, e.g.,* specification at page 12, line 12 through page 13, line 18); oligonucleotides and primers for obtaining oligonucleotides (*see, e.g.*, specification at page 9, line 22 through page 10, line 24 and in the sequence listing); oligonucleotides that hybridize to 3' untranslated regions (*see, e.g.* specification at page 21, line 17 through page 22, line 4 and in the sequence listing); and expression detection and quantitation methods (*see, e.g.*, specification at page 28, line 15 through page 37, line 9). Despite the numerous variations described for the nucleic acid molecules in the present specification, the Examiner argues that "the disclosure of a single sequence of SEQ ID NO: 2 is not representative of this genus." Office Action at page 3.

The purpose of the written description requirement is to ensure that the inventor had possession of the claimed subject matter, *i.e.*, to ensure that the inventor actually invented what is claimed. *Gentry Gallery Inc. v. Berkline Corp.*, 134 F.3d 1473, 1479,

45 U.S.P.Q.2d 1498, 1503 (Fed. Cir. 1998); *Lockwood v. American Airlines*, 107 F.3d 1565, 1572, 41 U.S.P.Q.2d 1961, 1966 (Fed. Cir. 1997); *In re Alton*, 76 F.3d 1168, 1172, 37 U.S.P.Q.2d 1578, 1581 (Fed. Cir. 1996). In accordance with this purpose, Applicants need not "describe," in the sense of Section 112, all things that are encompassed by the claims. To contend otherwise would contradict established jurisprudence, which teaches that a patent may be infringed by technology developed after a patent issues. *United States Steel Corp. v. Phillips Petroleum Co.*, 865 F.2d 1247, 1251, 9 U.S.P.Q.2d 1461, 1464 (Fed. Cir. 1989). A related, and equally well-established principle of patent law is that claims "may be broader than the specific embodiment disclosed in a specification." *Ralston Purina Co. v. Far-mor-Co*, 772 F.2d 1570, 1575, 227 U.S.P.Q. 177, 179 (Fed. Cir. 1985), *quoting In re Rasmussen*, 650 F.2d 1212, 1215, 211 U.S.P.Q. 323, 326 (C.C.P.A. 1981). Thus, simply because the claimed nucleic acid sequences may also include sequences from "other species, mutated fragment sequences, allelic variants, splice variants, genomic sequences and so forth" does not require that Applicants describe each and every one of these molecules.

In this regard, the written description requirement can be met by "show[ing] that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics...*i.e.,* complete or partial structure, other physical and or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics." *Enzo Biochem, Inc. v. Gen-Probe Inc.,* 323 F.3d 956, 964 (Fed. Cir. 2002). (quoting from Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description"

Requirement, 66 Fed. Reg. 1099, 1106 (Jan. 5, 2001)). Applicants have satisfied that test for written description. For example, Applicants have disclosed a structural feature, the nucleotide sequence of SEQ ID NO: 2. This feature provides a basis for each and every nucleic acid molecule in the claimed genus. Moreover, it distinguishes the members of the claimed genus from non-members.

The Examiner further alleges that "[w]hile the specification teaches examples of appropriate stringency hybridization conditions (page 13, lines 9-13), these examples do not connote structural limitation to the claims and as such it is not clear what resulting structure will occur from hybridization." Office Action at page 6. The Examiner again alleges that the "[e]ven stringent hybridization would tolerate mismatches and result in sequences that correspond to mutants, variants, and homologs of the 3' end of the *Pisum sativum* rbcS E9 gene which is not disclosed in the specification." *Id.* The Examiner concludes that the "specification only discloses a selected number of species of the genus; i.e. SEQ ID NO 2 (SEQ ID 7-9 and 28, which are part of SEQ ID NO 2), which is insufficient to put one of ordinary skill in the art in possession of all attributes and features of all species within the genus." *Id.* at pages 6-7. As discussed above, the skilled artisan is knowledgeable of the *P. sativum* rbcS E9 gene structure. A specification cannot fail to meet the written description requirement simply because it does "not re-iterate the structure or formula or chemical name" for known nucleotide sequences. *Capon v. Eshhar*, 418 F.3d 1349 (Fed. Cir. 2005).

In light of the detailed disclosure of the present application, one skilled in the art, after reading the present specification, would clearly know if a nucleic acid molecule

contains one of the recited nucleotide sequences. Thus, pending claim 50 is supported by an adequate written description pursuant to the requirements of 35 U.S.C. § 112. Reconsideration and withdrawal are respectfully requested.

IV. Rejection under 35 U.S.C. §102

Claims 35-37, 41-42, 45-46, and 48-50 are newly rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Fleming, *et al.*, *Plant Journal*, 1996, 10(4): 745-754.

Claims 35-37, 41-42, and 45-49 are newly rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Chelly *et al.*, *Nature*, 1998, 333: 858-860.

Claims 35, 41, 47, and 49 remain rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Hamilton, *et al. Gene*, 1997.

Applicants acknowledge and thank the Examiner for indicating that "[c]laim 40 has been found to be free of the cited prior art, but is objected to for being dependent on a rejected claim." Office Action at page 23. Applicants note that claim 51 presents the subject matter of claim 40 in independent form.

Applicants also acknowledge and thank the Examiner for indicating that "[c]laim 39, would be free of the cited prior art if amended" to read "[a] method according to claim 35, wherein said second transgenic nucleic acid molecule is the nucleic acid of SE ID NO: 2" as suggested by the Office. *Id.* Applicants note that new claim 52 presents the subject matter of claim 39 in independent form.

A. Fleming *et al.*, *Plant Journal*, 1996

Claims 35-37, 41-42, 45-46, and 48-50 stand rejected under 35 U.S.C. 102(b) as allegedly anticipated by Fleming *et al.* The Examiner asserts that:

> Fleming et al. teach reverse transcription of each rbcS gene (first transgenic nucleic acid) followed by PCR (instant claim 41-42) of the cDNA from each RNA sample using a common 5' primer for the coding region and a gene-specific 3' primer for each of the 3' UTR of the genes of rbcS.

Office Action at page 10.

"It is axiomatic that for prior art to anticipate under § 102 it has to meet every element of the claimed invention." *Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 231 U.S.P.Q. 81 (Fed. Cir. 1986). Further, "an anticipation rejection requires a showing that each limitation of a claim must be found in a single reference, practice, or device." *In re Donohue*, 766 F.2d 531, 226 U.S.P.Q. 619 (Fed. Cir. 1985).

Initially, Applicants disagree with the Examiner's characterization of the reference. In particular, the Examiner argues that "Fleming et al. teach a method of RT-PCR analysis of gene expression of rbcS genes in transgenic plants," and cites to the "summary and 2nd column, 1st paragraph, page 745" for support. However, nothing the Examiner cites to indicates that the plants analyzed by RT-PCR were transgenic. For example, the cited portion of the second column on page 745 recites that the authors "developed an RT-PCR analysis which would provide [the authors] with data on the time-dependent accumulation of specific RBCS transcripts during leaf primordium development." Moreover, the authors indicate that "the plant-to-plant variability in transgene expression for the five RBCS-GUS constructs analyzed made it difficult to discriminate differences in the level of promoter activity using fluorescent imaging of GUS activity." The authors go on to suggest that because of this plant-to-plant variability that "[w]ith the aim of identifying which *RBCS* genes were associated with the highest transcript levels at the

earliest stage of leaf development, we developed a semi-quantitative RT-PCR analysis of gene specific *RBCS* transcript levels." *Id.* The Examiner has not pointed to any support in Fleming that indicates that the RT-PCR was performed on nucleic acids obtained from transgenic plants.

Moreover, the disclosure of Fleming suggests that the nucleic acids for use in RT-PCR were obtained from non-transformed plants. For example, the Experimental procedures section of the reference states that "[f]or RT-PCR and *in situ* hybridization, seedlings of *Lycopersicon esculentum* cv. Moneymaker were grown in soil...." Fleming *et al.* at page 751, column 2. However, transgenic plants were indicated as the tissue source for other procedures discussed in the reference. For example, the authors indicate that "[f]or analysis of GUS expression by histochemical assay, immunocytochemistry and fluorescent imaging, *transgenic* F1 seeds were germinated and grown...." *Id.* (emphasis added). As such, the RT-PCR methods discussed in Fleming, *et al.* are not directed to detecting expression of a first transgenic nucleic acid molecule.

Moreover, Fleming *et al.* nowhere mentions hybridization to a second transgenic to indicate the expression of a first transgenic nucleic acid molecule. As the Examiner acknowledges, Fleming discusses the use of a "common 5' primer in the coding region" of the rbcS gene. Fleming, *et al.*, at page 752, Figure 5. Accordingly, the resulting amplification product includes sequence from the coding sequence of rbcS, or the first transgenic nucleic acid molecule, and therefore is not designed to hybridize to the second transgenic nucleic acid molecule. Hybridization with the resulting amplification product from the first nucleic acid would hybridize to itself. As such, the method discussed in

Fleming *et al.* is not used as a surrogate indicator for a first transgenic nucleic acid molecule.

The Examiner argues in the alternative that "Fleming et al. teach a method of semi-quantitative RT-PCR analysis of gene-specific rbcS transcript levels." Office Action at page 11. The Examiner argues that the cited reference teaches "that rbcS gene-specific transcript levels are expressed relative to the signal obtained using the RPL2 primers at corresponding sample dilutions (detecting expression of second transgenic nucleic acid which indicates expression of first transgenic nucleic acid)." *Id.* Applicants respectfully disagree with the Examiner's characterization of the reference.

Contrary to the Examiner's assertion that the "detecting expression of second transgenic nucleic acid which indicates expression of [the] first transgenic nucleic acid," the RPL2 amplification product is used as an internal control to determine the relative level of expression of the native rbcS gene. The Examiner has pointed to no evidence to support that either the rbcS or RPL2 sequence was transgenic.

In summary, whatever else Fleming *et al.* teaches, it does not disclose a method to detect the expression of a first transgenic nucleic acid molecule in sample comprising providing a complementary DNA of a mRNA transcribed from a second transgenic nucleic acid molecule. Absent a teaching of each and every element of the claims, the reference cited by the Examiner does not anticipate claims 35-37, 41-42, 45-46, and 48-50 and the rejection should be withdrawn.

Accordingly, for at least the foregoing reasons, the rejection of claims 35-37, 41-42, 45-46, and 48-50 under 35 U.S.C. § 102(b) is improper. Reconsideration and withdrawal of this rejection is respectfully requested.

B. Chelly *et al.*, *Nature*, 1998

Claims 35-37, 41-42, and 45-49 stand rejected under 35 U.S.C. 102(b) as allegedly anticipated by Chelly *et al.* Nature 1998, 333:858-860. The Examiner asserts that:

> Chelly et al. teach a method of co-amplification of mRNA of dystrophin gene (1st transgenic nucleic acid) and reporter gene, aldolase A, (second transgenic nucleic acid) (signal sequence, claim 37), by PCR (claim 41) which allows quantitative estimate of the dystrophin gene transcript (see abstract) (claim 41).

Office Action at page 12.

Again, Applicants respectfully disagree with the Examiner's characterization of the art. By way of example, the Examiner appears to assert that Chelly discloses the co-amplification of a transgenic dystrophin mRNA. Office Action at page 12. Further, the Examiner asserts that "Chelly et al. teach a pair of oligonucleotide primers and an oligonucleotide probe designed to hybridize to the second transgenic nucleic acid molecule." *Id.*

In this regard, Applicants note that nowhere does Chelly disclose or suggest the detection or quantitation of a first transgenic nucleic acid molecule. Rather, Chelly discusses the amplification of the native dystrophin and aldolase A transcripts from cDNA isolated from various human tissues. *See, e.g.*, Chelly, *et al.* at page 858, columns 1 and 2. Further, Applicants note that nowhere does Chelly disclose or suggest the detection or

quantitation of mRNA of a transgenic mRNA. The Examiner provides no teaching that the dystrophin or aldolase A genes are transgenic.

As such, whatever else Chelly *et al.* teaches, it does not disclose a method to detect the expression of a first transgenic nucleic acid molecule in sample comprising providing a complementary DNA of a mRNA transcribed from a second transgenic nucleic acid molecule. Absent a teaching of each and every element of the claims, the reference cited by the Examiner does not anticipate claims 35-37, 41-42, and 45-49 and the rejection should be withdrawn.

Accordingly, for at least the foregoing reasons, the rejection of claims 35-37, 41-42, and 45-49 under 35 U.S.C. § 102(b) is improper. Reconsideration and withdrawal of this rejection is respectfully requested.

C. Hamilton *et al.*, *Gene*, 1997

Claims 35, 40, 41, 47 and 49 remain rejected under 35 U.S.C. 102(b) as allegedly being anticipated by Hamilton *et al.* In support of this rejection, the Examiner asserts that:

> Hamilton demonstrates the expression of transgenes in a BIBAC vector (p. 113, 2nd column, 3rd paragraph), wherein a successful transfection into the host plant is determined based upon the following transgenic nucleic acids: *sacB* gene, GUS-NPTII gene (beta-glucuronidase – neomycin phosphotransferase II), and the HYP gene (hygromycin phosphotransferase). In one example, the first transgenic nucleic acid is the *sacB* gene and the second transgenic acid is the GUS-NPTII and/or HYG gene:
>
> Potential transgenic plants were initially tested by PCR using primers to the GUS-NPTII and HYG [...]. [...] Plants that tested positive for the BIBAC T-DNA by PCR [*thereby amplification, claim 35 step ii, and claim 41*] were all verified by Southern analysis [*thereby hybridization, claim 35 step iii, and claim 49*] using a

NPTII specific probe. (p. 113, 1st column, 3rd paragraph) (see also figure 3).

Office Action at page 13.

This rejection is respectfully traversed for at least the reasons which follow. As previously set forth, it is well established that to anticipate a claim, a reference must disclose every element of the claim. *Verdegaal Bros. v. Union Co. of California*, 2 U.S.P.Q.2d 1051, 1053 (Fed. Cir. 1987). The identical invention must be shown in complete detail as is contained in the claim. *Richardson v. Suzuki Motor Co.*, 9 U.S.P.Q.2d 1913 (Fed. Cir. 1989).

Applicant respectfully submits that the Hamilton *et al.* disclosure does not include all of the limitations of the present claims. Whatever else Hamilton *et al.* teaches, it does not disclose a method to detect the expression of a first nucleic acid molecule in sample employing, *inter alia*, providing a complementary DNA of mRNA transcribed from a second transgenic nucleic acid molecule. The Examiner has not pointed to any support that Hamilton discloses a method comprising providing a complementary DNA. Absent a teaching of each and every element of the claims, the reference cited by the Examiner does not anticipate claims 35, 36, 40-42 and 44-47 and the rejection should be withdrawn.

Moreover, Applicants maintain their disagreement with the Examiner's characterization of the reference. In particular, the Examiner asserts that "Hamilton teaches that plants that tested positive for BIBAC T-DNA by PCR were verified by southern analysis using a NPTII probe and southern analysis is a technique that detects expression of a sequence by hybridization of the probe." Office Action at page 14-15.

The skilled artisan would recognize that Southern analysis does not indicate the expression of the hybridized nucleic acid molecule. Moreover, as Hamilton discusses the Southern analysis was performed to verify that the BIBAC vectors described by Hamilton were integrated into the plant genome during transformation. As such, whatever else Hamilton *et al.* teaches, it does not teach a method to detect the expression of a transgenic nucleic acid molecule.

Accordingly, for at least the foregoing reasons, the rejection of claims 35, 36, 40-42 and 44-47 under 35 U.S.C. § 102(a) is improper. Reconsideration and withdrawal of this rejection is respectfully requested.

V. Rejection under 35 U.S.C. § 103

Claims 35-50 remain rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Hunt *et al.* (*DNA*, 1988), taken in combination with Freeman *et al.* (*BioTechniques*, 1999). This rejection is respectfully traversed for at least the reasons which follow.

To establish a *prima facie* case of obviousness, the prior art reference (or references when combined) must teach or suggest all of the claim limitations. There must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. The teaching or suggestion to make the claimed combination must be found in the prior art, and not be based on applicant's disclosure. *See* M.P.E.P. §§2143.01 and 2143.03.

In a proper obviousness determination, the changes from the prior art must be evaluated in terms of the whole invention, including whether the prior art provides any teaching or suggestion to one of ordinary skill in the art to make the changes that would produce the claimed invention. *See In re Chu,* 36 USPQ2d 1089, 1094 (Fed. Cir. 1995). This includes what could be characterized as simple changes. *See, e.g., In re Gordon,* 221 USPQ 1125, 1127 (Fed. Cir. 1984) (Although a prior art device could have been turned upside down, that did not make the modification obvious unless the prior art fairly suggested the desirability of turning the device upside down.).

Only when the prior art teaches or suggests the claimed invention does the burden fall on the applicant to rebut that *prima facie* case. *See In re Dillon,* 16 USPQ2d 1897, 1901 (Fed. Cir. 1990) (in banc), *cert. denied,* 500 U.S. 904 (1991). However, a *prima facie* case of obviousness may be rebutted by showing that the art, in any material respect, teaches away from the claimed invention.

The Office has not shown that the cited references teach or suggest the claimed invention. The Examiner argues that Hunt *et al.* discloses "the transformation of a tobacco plant with a plasmid carrying the 3' noncoding strand of the pea rbcS-E9 3' region (claims 37, 38) which aligns 99.5% with SEQ ID NO: 2 (a 637 bp sequence) from residue 1-633 (claim 39), and a desired transgene pAH10 (figure 2A)." Office Action at page 17. The Office acknowledges that Hunt *et al.*, however, "does not teach the amplification by PCR or RT-PCR, quantitative and competitive RT-PCR, the primers utilized for the amplification as required by claims 36, 41, 42, 47, 48 and 50." *Id.* at page 18.

The Examiner argues that "Freeman teaches the benefits of PCR, specifically utilizing quantitative RT-PCR, both competitive and non-competitive (pp. 116-117) to quantify mRNA (claims 36, 41, 42)." Office Action at page 18. Applicants respectfully submit that the cited references do not render the present independent claims obvious, since the claims are not taught nor suggested by the cited references. The cited references do not disclose or suggest a method to detect the expression of a first transgenic nucleic acid molecule in a sample comprising amplifying a complementary DNA from an mRNA from a second transgenic nucleic acid molecule and hybridizing the cDNA with at least one oligonucleotide designed to hybridize to the second transgenic nucleic acid molecule where hybridizing indicates the expression of the first transgenic nucleic acid molecule in a sample.

The Examiner has stated that "it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to improve the detection method of Hunt et al and further modify the mRNA expression analysis to utilize quantitative RT-PCR which includes amplification along with primers and probes designed for quantitative RT-PCR as per the teachings of Freeman et al. because Freeman teaches that quantitative RT-PCR provides increased sensitivity in mRNA detection." Office Action at page 11.

Initially, Applicants respectfully disagree with the Examiner's characterization of the art. By way of example, the Examiner asserts that "it would have been prima facie obvious ... to improve the detection method of Hunt, *et al*...." Office Action at page 18. In this regard, Applicants note that nowhere does Hunt *et al.* disclose or suggest a method

for detecting the expression of a first transgenic nucleic acid molecule. As previously discussed, Hunt, *et al.* faced the problem of identifying sequence requirements for the polyadenylation of mRNAs in plants. The cited reference shows "that the 3' region of the pea *rbcS*-E9 gene has a number of discrete, cryptic polyadenylation sites located downstream from the previously-determined poly(A) sites of this gene." Hunt, *et al.*, at page 329, second column, last sentence. The Examiner has not cited any support for the proposition that the methods discussed in Hunt were not sufficient to solve the problem faced in Hunt and would therefore require improvement. As such, it is respectfully submitted that the Examiner's conclusion of obviousness is based on improper reasoning and a misinterpretation of the art.

Moreover, the modification of Hunt, *et al.* proposed by the Examiner would render the reference unsatisfactory for its intended purpose. *See,* MPEP 2143.01. Hunt *et al.* discusses that "[t]he sequence requirements for the polyadenylation of mRNAs in plant have not been carefully studied." Hunt et al. page 329, Second column. S1 nuclease protection analysis was performed to identify 3' ends in the rbcS 3' region. *Id.* at page 332, paragraph spanning columns 1 and 2. Modifying Hunt *et al.* as suggested by the Examiner to use RT-PCR would not identify 3' ends.

Even assuming *arguendo* that the combination is proper, the combination does not render the claimed invention obvious. Whatever else Hunt *et al.* and Freeman *et al.* disclose, the do not teach or suggest a method to detect the expression of a first transgenic nucleic acid molecule in a sample by hybridizing a complementary DNA of mRNA transcribed from a second transgenic nucleic acid molecule with at least one

oligonucleotide designed to hybridize to the second transgenic nucleic acid molecule where the hybridization indicates the expression of the first transgenic nucleic acid molecule in the sample. The Examiner has not pointed to any specific suggestion in any of the cited references to reach the presently claimed invention. It is impermissible hindsight to find it obvious for one skilled in the art to combine the cited references to reach the invention in the present application absent some suggestion or motivation in the cited references. Therefore, it would not be obvious to one skilled in the art, from reading Hunt *et al.* and Freeman *et al.* that one could obtain the methods of the present invention.

Moreover, the skilled artisan would not turn to Hunt *et al.* to solve the problem of detecting the expression of a first transgenic nucleic acid molecule. "In order to rely on a reference as a basis for rejection of an applicant's invention, the reference must either be in the field of applicant's endeavor or, if not, then be reasonably pertinent to the particular problem with which the inventor was concerned." *In re Oetiker*, 977 F.2d 1443, 1446, 24 USPQ2d 1443, 1445 (Fed. Cir. 1992). *See also In re Deminski*, 796 F.2d 436, 230 USPQ 313 (Fed. Cir. 1986); *In re Clay*, 966 F.2d 656, 23 USPQ2d 1058 (Fed. Cir. 1992). Applicants submit that Hunt *et al.* is not analogous art. First, the Hunt *et al.* reference is not in the Applicant's field of endeavor. The Hunt *et al.* reference describes the identification of "a number of discrete, cryptic polyadenylation sites located downstream from the previously-determined poly(A) sites of" the 3' region of the pea *rbcS*-E9 gene. This is a different field of endeavor from the methods for detecting the expression of a first transgenic nucleic acid molecule in a sample by hybridizing a complementary DNA of mRNA transcribed from a second transgenic nucleic acid molecule with at least

one oligonucleotide designed to hybridize to the second transgenic nucleic acid molecule where the hybridization indicates the expression of the first transgenic nucleic acid molecule in the sample.

Nor is Hunt *et al.* reasonably pertinent to the particular problem that the present inventors faced. Hunt *et al.* addresses the structural "sequence requirements for the polyadenylation of mRNAs in plants." Hunt, page 329. A person faced with the problem of detecting or quantifying the expression of a first transgenic nucleic acid molecule would not find the teachings of Hunt pertinent. Hunt does not address the problem of detecting or quantifying the expression of a transgenic nucleic acid sequence, but rather addresses the structural requirements for polyadenylation.

Moreover, Freeman *et al.* does not make up what Hunt lacks. The Examiner argues that Freeman *et al.* "teaches designing primers for use in [quantitative RT-PCR assays] to be gene specific or non-specific however if specific then it 'increases specificity and decreases background associated with other types of primers.'" Office Action at page 11. Applicants submit that Freeman *et al.* further describe non-specific primers as "[r]andom hexamer primers [containing] all possible nucleotide combinations of a 6-base oligonucleotide and bind to all RNAs present," and "oligonucleotides solely of deoxythymidine residues [oligo(dT)]." The cited reference does not disclose a method for detecting the expression of a first transgenic nucleic acid molecule in a sample by hybridizing a complementary DNA of mRNA transcribed from a second transgenic nucleic acid molecule with at least one oligonucleotide designed to hybridize to the second transgenic

nucleic acid molecule where the hybridization indicates the expression of the first transgenic nucleic acid molecule in the sample.

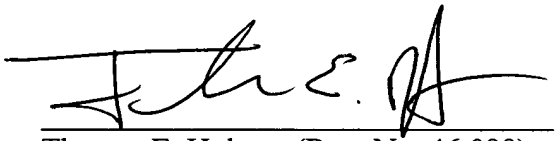
In sum, the Examiner's conclusion of obviousness is based on improper hindsight reasoning. "Impermissible hindsight must be avoided and the legal conclusion must be reached on the basis of the facts gleaned from the prior art." M.P.E.P. § 2142 at 2100-124. No suggestion to modify the cited references has been found in the cited references or pointed out to Applicant from the general knowledge of one of ordinary skill in the art. In addition, no indication for Hunt *et al.* teaching the claimed method is provided. For at least these reasons, the Applicant respectfully submits that the Examiner has failed to establish a *prima facie* case of obviousness, as required by 35 U.S.C. § 103.

Accordingly, for at least the foregoing reasons, the rejection of claims 35-50 under 35 U.S.C. § 103 is improper. Reconsideration and withdrawal of this rejection are respectfully requested.

Conclusion

In view of the foregoing remarks, Applicants respectfully submit that the present application is now in condition for allowance, and notice of such is respectfully requested. The Examiner is encouraged to contact the undersigned should any additional information be necessary for allowance.

Respectfully submitted,



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